CONCERNING THE EFFECT OF CIRCULATORY DISTURBANCES AND EDEMA OF THE LUNGS ON THE ETIOLOGY AND COURSE OF THE INFECTIOUS PROCESS IN THEM (PNEUMONIA)

I. THE EFFECT OF INTRAPERITONEAL ADMINISTRATION OF ADRENALIN ON THE DEVELOPMENT OF EXPERIMENTAL PNEUMOCOCCUS PNEUMONIA IN WHITE RATS

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The works of I. P. Pavlov [12], S. P. Shakh-Paronian [25], N. N. Anishkov and M. A. Zakhar'evskaya [1,2] and especially the investigations of many years by V. D. Tsinzerling [22] and his coworkers demonstrated that in the etiology of pneumonia of great importance are disturbances in the activity of the protective mechanisms of the respiratory organs which create conditions for the infection of the lungs. At the same time, changes in the state of the organism and of the pulmonary tissue determine to a certain extent the possibility of the development of infectious processes in the lungs. Among pulmonary changes many authors [3,13,16,19,23,24,27,29] indicate disturbances of circulation and edema which, in their opinion, represent the leading factors in the pathogenesis of pneumonia. However, the role of circulatory disturbances in the lungs in the mechanism of development of pneumonia remains obscure at present; yet, the solution of this problem is of importance not only in regard to pneumonia, but in relation to the infectious process in general.

We conducted special experimental investigations aimed at the study of the development and course of pneumonia in circulatory disturbances in the lungs of white rats.

METHOD

We employed adrenalin to obtain pulmonary edema, since many authors point to the fact that its administration induces circulatory disturbances in the pulmonary tissue and its edema [5,17,18,30,32, etc.].

Preliminary investigations, carried out on 65 white rats, showed that 0.1% of an adrenalin solution introduced intraperitoneally in the amount of 0.5 ml per 100 gm of the animal's body-weight causes a rapid death of almost all animals. At a reduced dosage (0.3 ml per 100 gm) the majority of animals survives. Under these conditions their lungs reveal circulatory changes which attest to the impairment of permeability of the vascular wall: hyperemia bleeding, perivascular and sometimes an alveolary edema.

Basic experiments were carried out according to the following method: White rats, slightly stunned with ether, were given intrasally 10 drops of an 18-hour broth culture of the type III pneumococcus in 1:2 dilution (75,000,000 microbial bodies) according to the method employed by V. N. Fadeeva and V. Ya. Fel' [20] with the same pneumococcus strain. After the animals had completely recovered from the dazed state (within 10-15 minutes) they were injected intraperitoneally with a 0.1% solution of adrenalin as per calculation of 0.3 ml per 100 gm of body weight. As control served white rats of the same weight which received no adrenalin after having been infected. A total of 60 rats were used in the experiment. Within $1^1/_2$,4,24,48,96, and 120 hours after infection the animals were killed. Pulmonary tissue was obtained for histological examination; the celloidin-paraffin slides from the pulmonary tissue were stained by the Nicoll method for the elicitation of the microorganisms. In addition, we used staining with hematoxylin-eosin and azan as per Heidenhein. For the elicitation of the topographic relationships we used a microprojector and a comparison microscope.

RESULTS

The results of our experiments showed that the pneumonia rate in both groups of animals is identical (Table 1). However, the onset of the pneumonic process in the experimental animals would start later, the inflammation foci at

all periods, especially during the first 48 hours, were considerably less pronounced than in the control rats, and the nature of inflammatory changes and their dynamics corresponded to the data obtained by V. N. Fadeyeva and V. Ya. Fel' [20].

Upon bacterioscopic examination of the lungs, attention was drawn to the fact that in the inflammatory foci of the experimental animals during the first 48 hours the number of free microorganisms was considerably lower than in the control rats. To obtain more precise data, we staged bacteriological tests on 10 rats, five of which received adrenalin. Within 30 minutes following adrenalin injection (40 minutes after infection) all animals were killed. The material from the lungs was inoculated on Petri dishes with 5% blood agar. After a 24-hour exposure of the dishes in a thermostat, the grown colonies were counted. In addition, another analogous experiment was carried out on 10 animals where the animals were killed within six hours after infection. The results are shown in Table 2.

TABLE 1. The Dynamics of Pneumonia Development in Experimental and Control Animals

Number of animals	Time, hours	Number of animals afflicted with pneumonia			
		Upon macroscopic exam.		Upon microscopic exam.	
		Experiment	Control	Experiment	Control
	1½-4	-	-	1	4
	24	1	2	4	4
	48	3	5	6	6
	96	5	5	5	5
12	120	5	2	5	2
Total		14	14	21	21

As seen in Table 2, after infection there was observed a reduction of the number of viable microorganisms in the lungs of both animal groups. It is clearly seen, however, that this reduction was much more considerable in animals which had been given adrenalin, from the lungs of which nearly 3-fold less microorganisms were isolated than from the lungs of control rats. A similar ratio was preserved also during the latter stages (within six hours). However, the rate of microbial growth in the experimental and control groups was approximately the same.

TABLE 2. General Data on the Quantity of Viable Microorganisms in the Lungs of Experimental and Control White Rats

Number of the experiment	Infecting dose (in millions of microbial bodies)	Time after infection	The quantity of viable microbial cells in the lungs (in millions)	
			Expt.	Control
1	154	30 Min.	2,8	8,2
2	154	6 Hr.	19,6	66,9

In the light of the cited data, the retardation of development of the infectious process in the lungs of experimental animals becomes understandable. Apparently, in order to develop a pneumonic process similar to the one in control animals, more time was needed for the proliferating bacilli to reach a sufficient degree of growth.

Thus the obtained data clearly demonstrated that the injection of adrenalin which impaired pulmonary circulation did not contribute, but actually inhibited the development of the pneumonic process. These data are not contradicted by the fact that within 120 hours in four out of the six control animals no pneumonic development was observed. In the experiments of V. N. Fadeeva and V. Ya. Fel' [20], conducted similarly to our experiments, also not every animal contracted pneumonia. Apparently, toward the 6th day some control animals survived and no pneumonia developed or was mildly expressed, whereas animals with a marked inflammatory process in the lungs perished as early as within 96 hours (five out of six). On the other hand, in the experimental rats toward the 6th day pneumonia was only reaching its full development.

It is more difficult to explain the reason why an adrenalin injection leads to a reduction of the number of introduced microorganisms to a much greater extent than under ordinary conditions.

At present we can only express a tentative opinion.

Although adrenalin represents a sympathicotropic substance, many authors [4,7,8,31, et al.] report that upon its introduction a transitory excitation of the nn. vagi centers is observed, through which the basic correcting influence of the central nervous system is affected on the activity of the protective mechanisms of the respiratory organs [11, 12,27,28,33]. The rise in the tonus of nn. vagi has a particular effect on the functions of the ciliary epithelium where the ciliary movements show a marked increase [9,10,15,26]. In comparing these data with our results, it is possible to assume that some of the introduced microorganisms could have been eliminated rapidly from the organs of respiration thanks to the enhanced functioning of the protective mechanisms of the tracheobronchial tree.

On the other hand, the reduction of the number of microorganisms in the lungs of experimental animals could also depend on their more rapid destruction by the cellular elements (macrophages and leucocytes) the phagocytary activity of which increases considerably under the effect of adrenalin, as our experiments have demonstrated as well as special investigations of other authors [6,14,21, et al.].

The adrenalin effect on the centers of nn. vagi and its stimulation of phagocytosis are very transitory, which apparently explains the fact that these influences are manifested only at the start. This has been confirmed to a certain extent by our observations where the growth rate of the microorganism in the experiments and control proved to be indentical.

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